ISSN 2706-6819 Vol. 7, Issue 1: 26-31, DOI: 10.25236/IJFM.2025.070105

Analysis of Genetics-Environmental Factors Interaction in Childhood Asthma

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Abstract: *Childhood asthma is a complex multifactorial disease whose pathogenesis is influenced by a combination of genetics and environmental factors. In recent years, there has been a gradual increase in studies on the interaction between genetic susceptibility and environmental exposures, revealing how the two work together in the development and progression of asthma. The aim of this study was to investigate the genetic basis of childhood asthma and the influence of environmental factors, and to analyze the mechanism of their interaction. By reviewing relevant literature and clinical studies, this paper summarizes the discovery of asthma susceptibility genes and the influence of environmental factors on asthma development. The study also discusses the potential application of gene-environment interaction modeling in the prediction and treatment of childhood asthma. Finally, the paper points out the challenges in current research and future research directions, especially how to achieve individualized prevention and treatment strategies through precision medicine. Through a deeper understanding of the interaction between genetics and environmental factors in childhood asthma, it is expected to provide a new theoretical basis and practical guidance for the early diagnosis and intervention of this disease.*

Keywords: *childhood asthma, genetics, environmental factors, gene-environment interaction, air pollution, lifestyle, allergic reactions, socioeconomic factors*

1. Introduction

Childhood asthma is one of the most common chronic diseases worldwide, affecting the health and quality of life of a large number of children[1]. According to the World Health Organization, asthma has become a major respiratory disease in childhood, and its incidence is on the rise in many countries. The etiology of asthma has not yet been fully clarified, and studies have shown that genetic and environmental factors play an important role in the onset and development of asthma[2]. Genetic studies have found that childhood asthma is often associated with specific susceptibility genes, yet the expression and function of these genes are often regulated by external environmental factors[3]. Environmental pollution, allergen exposure, lifestyle habits and socio-economic factors have all been recognized as key triggers of asthma.

In recent years, more and more studies have focused on the interactions between genetic and environmental factors, especially the effects of gene-environment interactions on the development of asthma in children[4]. Existing studies still face many challenges, including the diversity of environmental factors, the complexity of genetic susceptibility, and the mechanisms of their interactions are not fully understood. Therefore, an in-depth exploration of how genetics and environmental factors interact and jointly influence the development of childhood asthma is an important direction for current research[5]. In this paper, we will analyze the genetic basis of childhood asthma and environmental factors, and explore the interaction between them, with the aim of providing theoretical support and practical guidance for the early prevention and precise treatment of asthma[6].

2. Genetic basis of childhood asthma

The genetic basis of childhood asthma is one of the key factors in understanding the pathogenesis of the disease[7]. Studies have shown that the development of asthma in children is closely related to genetic susceptibility, especially in children with a family history of asthma, the risk of asthma is significantly increased. Twin and family lineage studies have shown a high heritability of asthma, and genetic factors are estimated to account for 30% to 60% of the development of asthma[8]. Although

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genetic factors play an important role in the development of asthma, environmental factors also play a non-negligible role; therefore, the development of asthma in children is often the result of a combination of genetic susceptibility and environmental exposure. Genetic susceptibility model (e.g., additive genetic model):

$$P(\text{Asthma}) = \alpha + \beta_1 G_1 + \beta_2 G_2 + \cdots + \beta_n G_n \quad (1)$$

With the development of genomics technology, scientists have identified a series of genes associated with childhood asthma. Most of these genes are closely related to aspects of the immune system, allergic response and airway inflammation[9]. genes for cytokines, such as IL-4, IL-13 and TNF-α, have been associated with asthma susceptibility and clinical manifestations, and mutations in the Filaggrin gene have also been implicated as an important genetic factor in allergic asthma[10]. Through genome-wide association analysis (GWAS), researchers have identified more genetic variants associated with the development of asthma. These findings provide new ideas for the genetic study of asthma and may provide new targets for early diagnosis and treatment of the disease, showed in Figure 1 :

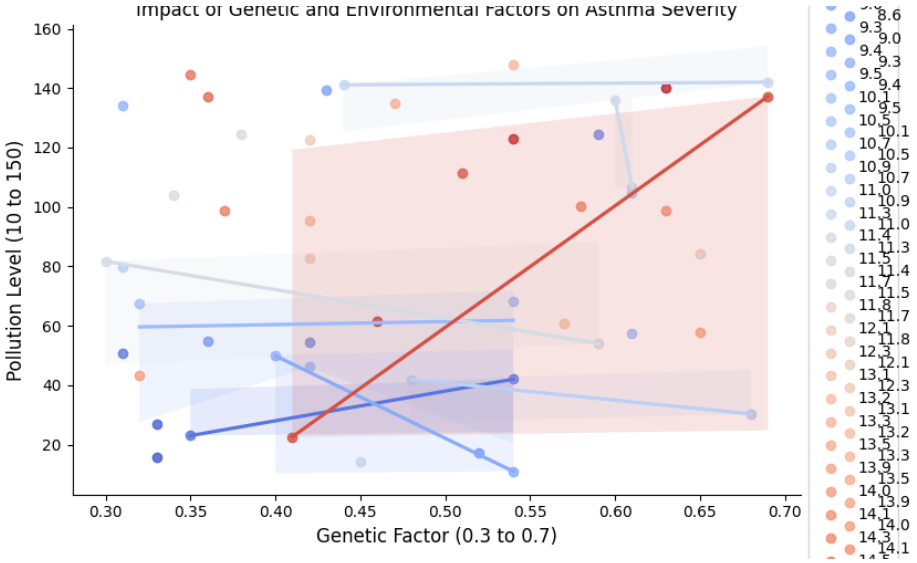

Figure 1: Impact of Genetic and Environmental Factors on Asthma Severity

The function of the immune system is closely related to the development of asthma in children, and genetic factors play a decisive role in the pathogenesis of asthma by regulating the immune response. It has been found that the immune system of asthmatics usually exhibits an overreaction to certain external stimuli (overreactions. These immune responses usually involve T cells, IgE antibody production, and airway epithelial cell reactivity. Genetic variations may lead to abnormal activation of immune pathways, making children more susceptible to excessive immune responses when exposed to specific environmental factors, which can trigger asthma attacks.

Genetic factors have an important role in the development of asthma in children, and genetic susceptibility is not sufficient to fully explain the complex etiology of asthma. Environmental factors, air pollution, allergens, and home living environment often interact with genetic susceptibility to promote asthma. Gene-environment interactions have become an important direction in current asthma genetics research. Certain genetic susceptibility genes may make individuals more susceptible to triggering an immune response in response to specific environmental exposures. Conversely, alterations in certain environmental factors, especially in the case of early exposure, may also have long-term effects on the immune system of genetically susceptible individuals. Understanding the interaction between genetic and environmental factors is essential for a comprehensive understanding of the pathogenesis of childhood asthma.

3. Influence of environmental factors on childhood asthma

Environmental factors play a crucial role in the onset and development of childhood asthma. Studies have shown that air pollution, allergen exposure, lifestyle and home environment are closely related to the development of asthma. Air pollutants such as particulate matter and nitrogen oxides can

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exacerbate airway inflammation and increase the risk of asthma; allergens, such as pollen, dust mites, and pet dander, can trigger or exacerbate allergic asthma; and lifestyle, such as dietary habits, physical activity, and socio-economic factors, can influence the development of asthma in children through a variety of pathways. These environmental factors interact with each other through different mechanisms, affecting the function of the immune system and thus inducing the manifestation of asthma symptoms in different individuals.

3.1. Air pollution and allergic reactions

Air pollution and allergic reactions are closely related in the development of childhood asthma. Studies have shown that airborne pollutants such as particulate matter (PM2.5), nitrogen oxides (NOx), and sulfur dioxide (SO2) can exacerbate the inflammatory response in the airways, leading to increased asthma symptoms in children. When pollutants enter the airways, they can trigger a series of immune responses that activate airway epithelial cells and inflammatory pathways of the immune system, thus making the airways more susceptible and increasing the frequency and severity of asthma attacks. In particular, children chronically exposed to high levels of air pollutants have significantly higher asthma incidence and symptom severity than children living in clean environments. Gene-environment interaction model:

$$P(\text{Asthma}|G,E) = \alpha + \beta_1 G + \beta_2 E + \beta_3 G \times E \tag{2}$$

Air pollution does not only affect the airways through direct physicochemical effects, but can also play an important role in allergic reactions by altering the immune response. It has been found that air pollutants may enhance the occurrence of allergic reactions by affecting the function of immune cells such as T cells and B cells. Particularly in allergic children, air pollutants may promote allergic inflammation by increasing the levels of antibodies to IgE, a key immune marker of allergic reactions. air pollutants may cause exacerbation of asthma symptoms by activating the allergic pathway of the immune system, making children more sensitive to common allergens such as pollen and dust mitesm, showed in Figure 2 :

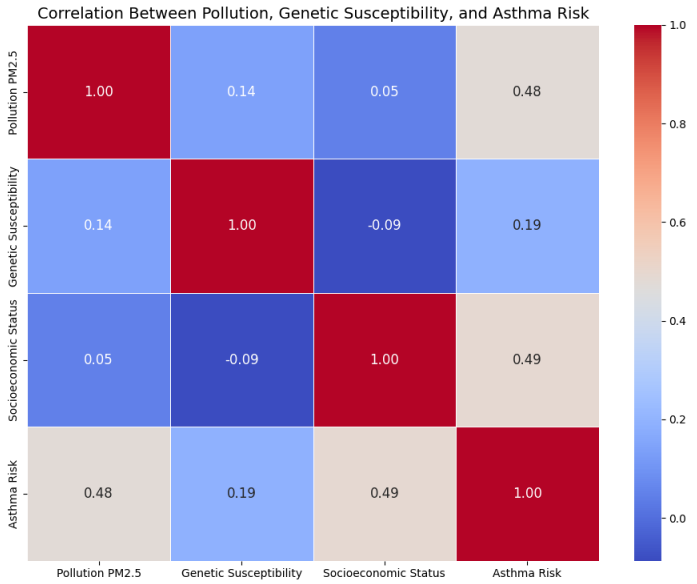

Figure 2: Correlation Between Pollution, Genetic Susceptibility, and Asthma Risk

Air pollution is also capable of altering the respiratory microecology, further affecting the allergic response. Recent studies have found that air pollution can alter the composition of the respiratory microbial community, leading to an increase in harmful flora and disrupting normal immune regulatory mechanisms. These changes may prompt the immune system to produce an excessive inflammatory response, thus making allergy symptoms more likely to appear and worsen. Particularly in infancy and early childhood, the establishment of respiratory microbial communities is closely related to the development of asthma, and air pollution increases the risk of asthma in children by affecting the microecological balance. Air pollution not only exacerbates the inflammatory response of the airways, but also enhances the occurrence of allergic reactions through multiple pathways, especially in allergic

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children. Therefore, reducing the emission of air pollutants and improving air quality, especially for the protection of children, will be one of the effective measures to reduce the incidence of childhood asthma and alleviate its symptoms.

3.2. The Role of Lifestyle and Diet

There is increasing interest in the impact of lifestyle and dietary habits on childhood asthma, and studies have found that they play an important role in the development and progression of asthma through a variety of mechanisms. Physical inactivity and a sedentary lifestyle have been shown to be among the risk factors for the development of asthma in children. Lack of adequate physical activity weakens the normal functioning of the immune system and increases the inflammatory response in the airways, leading to an exacerbation of asthma symptoms. In contrast, moderate exercise strengthens lung function, improves airway ventilation, and helps regulate the immune response, thereby reducing asthma symptoms. Encouraging children to maintain an active lifestyle and increase outdoor activities may help reduce the occurrence of asthma and relieve existing symptoms.

The impact of dietary habits on childhood asthma should not be overlooked. The high-fat, high-sugar and low-fiber nature of the modern diet may contribute to the development and exacerbation of asthma. A high-fat diet promotes an increased inflammatory response in the body, leading to airway hyperresponsiveness, which can trigger or exacerbate asthma. And diets lacking adequate fruits, vegetables and fiber may make children's immune systems more susceptible to external allergens, increasing susceptibility to asthma. Studies have also shown that certain antioxidant-rich foods, fresh vegetables and fruits, can help reduce asthma symptoms by reducing airway inflammation through anti-inflammatory effects.

In addition to the type of food, the timing and manner of eating may also affect the risk of asthma in children. Eating too quickly or consuming too much processed food may lead to gastrointestinal distress, which may indirectly affect respiratory health. Further studies have found that the duration of breastfeeding in infancy is significantly associated with the risk of developing asthma. Immune factors and anti-inflammatory substances in breast milk strengthen the infant's immune system and help reduce the incidence of asthma. In contrast early introduction of artificial feeding increases the risk of asthma, especially in children with a genetic predisposition.

Certain lifestyle habits in the environment may also indirectly affect the development of asthma by influencing the health status of children. Smoking in the home is a known risk factor for asthma, and secondhand smoke can increase the incidence of asthma in children and exacerbate its symptoms. Prolonged exposure of children to harmful substances such as smoke and air pollution may lead to immune system dysfunction and increase allergic and inflammatory responses in the airways. Promoting a smoke-free environment, reducing exposure to air pollution and developing healthy living habits are important measures to reduce the incidence of asthma in children.

3.3. Family environment and socio-economic factors

Family environment and socioeconomic factors play an important role in the occurrence and development of childhood asthma. The hygienic conditions of the home environment, the air quality of the living environment, and the health habits of family members all directly or indirectly influence the risk of childhood asthma. Allergens in the home (e.g., pets, dust mites, molds, etc.) are one of the major triggers of asthma. Children exposed to these allergens for a long period of time are prone to an overreaction of the immune system, which can lead to the onset of asthma and exacerbation of symptoms. Factors such as air pollution, smoke and kitchen fumes in the home environment may increase the inflammatory response in the airways, leading to the frequency and severity of asthma attacks. Studies have shown that children living in environments with high levels of air pollution, high humidity or poor sanitation have a significantly higher incidence of asthma than children living in good environments.

Family economic status and parents' education level are also strongly associated with the development of asthma in children. Children from low-income families are more likely to be exposed to poor living conditions, lack of adequate nutrition, poorer housing environments, and limited medical resources. These factors may lead to a poorly functioning immune system in children, increasing the risk of asthma. Children from low-income families may not have access to adequate medical support and asthma management, leading to exacerbation of asthma symptoms. Parents' education level is also associated with the ability to manage asthma in children. More highly educated parents are more likely

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to be aware of asthma prevention and management measures and are able to provide more appropriate diet, exercise and environmental conditions to reduce asthma triggers.

Socioeconomic factors not only affect the economic status of the family, but are also closely related to children's lifestyle, nutritional status and health management. Families with low socioeconomic status often do not have access to quality healthcare services, and children's asthma conditions may be exacerbated by untreated or poorly managed asthma. At the same time, low socioeconomic status is often accompanied by poor living conditions and high levels of environmental pollution, which pose potential threats to children's health. Studies have also found that low-income children may face additional challenges in terms of stress, mental health, and other factors that may also have an impact on the development of asthma.

Socioeconomic factors also influence the implementation of public health policies and environmental protection efforts. In more economically developed areas, governments often increase monitoring and improvement of air quality and promote public health programs, which can help reduce the incidence of asthma. However, in less economically developed regions, the lack of environmental protection and public health resources may result in more children being exposed to unfavorable environmental conditions, increasing the risk of asthma. Therefore, improving the home environment, upgrading socioeconomic conditions, and especially providing better healthcare services and environmental protection measures are essential to reduce the incidence of asthma in children.

4. Genetic-environmental interactions

The interaction between genetics and the environment plays a key role in the pathogenesis of childhood asthma. While genetic factors provide the basis for susceptibility to asthma, exposure to environmental factors is often the trigger that initiates or exacerbates asthma. This gene-environment interaction explains why some genetically susceptible children exhibit asthma symptoms only in response to specific environmental factors, while some may not develop the disease even in the presence of higher environmental exposures. Studies have shown that environmental factors such as air pollution, allergens, and dietary habits can promote or inhibit the development of asthma by modulating gene expression or affecting the function of the immune system.

Environmental factors may enhance genetic susceptibility by affecting gene expression. Air pollutants (e.g., PM2.5, nitrogen oxides, etc.) can activate inflammatory pathways in the airways, contributing to the upregulation of asthma-related gene expression, which can lead to enhanced airway inflammation and immune responses. Specifically, air pollutants can make allergic reactions more severe by altering the activity of immune cells, especially in children who are genetically susceptible, and these pollutants can further promote asthma symptoms. Certain environmental exposures such as smoking or viral infections may also alter gene expression patterns through epigenetic mechanisms, which in turn may affect immune responses and airway function in children.

Variations in genes may determine a child's susceptibility to environmental factors. In genetically susceptible individuals, certain gene mutations increase the risk of asthma by making their immune system more sensitive to environmental exposures. Children with specific genetic variants may be more likely to have allergic reactions to allergens such as pollen and dust mites, leading to asthma attacks. Whereas in individuals without these genetic variants, exposure to the same environmental factors may not cause an allergic reaction or the onset of asthma symptoms. This gene-environment interaction makes the clinical manifestations of asthma highly individualized.

Gene-environment interactions are particularly important in early childhood development. The immune system is still developing in childhood, and environmental exposures have a more profound effect on the immune system. Early exposure to air pollution, allergens, or certain unhealthy diets may alter airway development patterns by affecting gene expression and immune system development, making children more susceptible to asthma. Research also suggests that feeding practices and environmental factors during infancy, duration of breastfeeding, and smoking in the home may reduce a child's risk of developing asthma in the future by influencing the early development of the immune system. Thus, early gene-environment interactions are critical to the development of asthma.

Understanding genetic-environmental interactions will not only help to unravel the pathogenesis of asthma, but may also provide new strategies for prevention and treatment. By developing personalized environmental interventions for genetically susceptible individuals, reducing air pollution exposure, avoiding allergen exposure, and improving dietary habits may be effective in reducing the occurrence

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of asthma or alleviating its symptoms. Future studies may provide important clues for the development of new drugs or therapeutic regimens by identifying specific gene-environment interaction patterns. Genetic-environmental interactions are key to understanding the complexity of childhood asthma and developing precise treatment strategies.

5. Conclusion

The development of childhood asthma is closely related to genetic and environmental factors, which together determine the susceptibility and pathogenesis of asthma through complex interactions. Genetic factors provide the basis of individual susceptibility, while environmental factors trigger or exacerbate asthma symptoms under specific conditions. Studies have shown that factors such as air pollution, allergen exposure, lifestyle, dietary habits, and home environment all play an important role in the onset and development of asthma, especially when these environmental factors interact with genetic susceptibility, the risk of asthma increases significantly. Prevention and treatment of childhood asthma should be approached from both genetic and environmental perspectives, emphasizing the interaction between an individual's genetic susceptibility and environmental factors. Improving air quality, reducing allergen exposure, and encouraging healthy lifestyles and diets will help reduce the incidence of childhood asthma. In particular, early intervention to improve the home environment, avoid bad habits, and reduce the impact of environmental pollution through personalized preventive measures are important for asthma prevention.

Future studies should further explore the specific mechanisms of gene-environment interaction, identify more asthma-related genetic markers, and combine the technological tools of big data and precision medicine to provide new ideas and strategies for early diagnosis and personalized treatment of asthma. Understanding and exploring the interaction between genetic and environmental factors will provide important theoretical support and practical guidance for the prevention, control and treatment of childhood asthma.

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